

12

EUROPEAN PATENT APPLICATION

21 Application number: 87100614.4

22 Date of filing: 19.01.87

91 Int. Cl. 4: **C07D 249/08** , **C07D 233/60** ,
A01N 43/653 , **A01N 43/50** ,
C07C 67/343 , **C07C 120/00**

30 Priority: 23.01.86 IT 1916986

43 Date of publication of application:
02.09.87 Bulletin 87/36

84 Designated Contracting States:
AT BE CH DE ES FR GB GR LI NL SE

71 Applicant: Montedison S.p.A.
31, Foro Buonaparte
I-20121 Milan(IT)

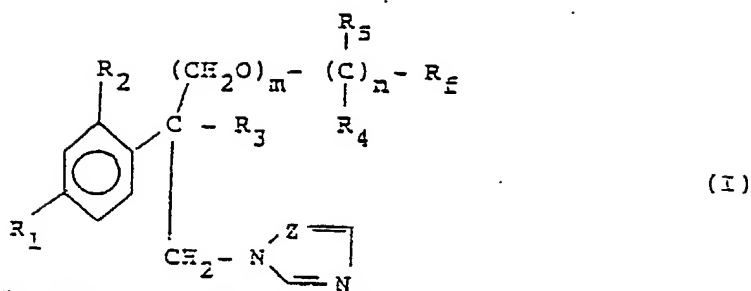
72 Inventor: Colle, Roberto Dr.
821, Residenza Parco Milano 3
I-20089 Basiglio Milan(IT)
Inventor: Corda, Francesco
13, via Teodosio
I-20131 Milan(IT)
Inventor: Camaggi, Giovanni Dr.
32, via Defendente
I-20075 Lodi Milan(IT)
Inventor: Gozzo, Franco Dr.
36/b, via Pascoli
I-20097 S. Donato Milanese Milan(IT)
Inventor: Mirena, Luigi
4, via Gambolotta
I-20139 Milan(IT)
Inventor: Garavaglia, Carlo
7, piazza Vittoria
I-20012 Cuggiono Milan(IT)

74 Representative: Weinhold, Peter, Dr. et al
Patentanwälte Dipl.-Ing. G. Dannenberg Dr.
P. Weinhold Dr. D. Gudel Dipl.-Ing. S.
Schubert Dr. P. Barz Siegfriedstrasse 8
D-8000 München 40(DE)

EP 0 234 242 A2

54 Fungicidal azolyl-derivatives.

57 Disclosed are compounds, having the general formula:



as well as corresponding salts or metal complexes, wherein:

$\underline{m} = 0, 1$; $\underline{n} = 0, 1$;

Z = CH, N;

R₁ is selected from chlorine, bromine, fluorine, CF₃, phenyl, C₁-C₂-alkoxy, C₁-C₂-haloalkoxy, alkylthio, haloalkylthio wherein the halogen is Cl, Br, F;

R₂ is H, fluorine, chlorine, bromine;

R₃ represents H, CH₃, CN, or also F when $\underline{m} = 1$ or when $\underline{n} = 1$ and R₄, R₅ are H;

R₄, R₅ are independently H or F;

R₃ and R₄, when $\underline{m} = \underline{n} = 1$, can furthermore represent, taken together, a second bond between the two carbon atoms to which they are linked in formula (I);

R₁ is selected from the group formed by polyfluoroalkyls, polyfluoroalkenyls and polyfluoroalkynyls containing up to 4 carbon atoms, containing at least 2 F atoms and, optionally, other halogens selected from Cl and Br.

FUNGICIDAL AZOLYL-DERIVATIVES.

The present invention relates to azolyl-derivatives endowed with high fungicidal activity, to the process for their preparation, and to their related use in the agrarian field.

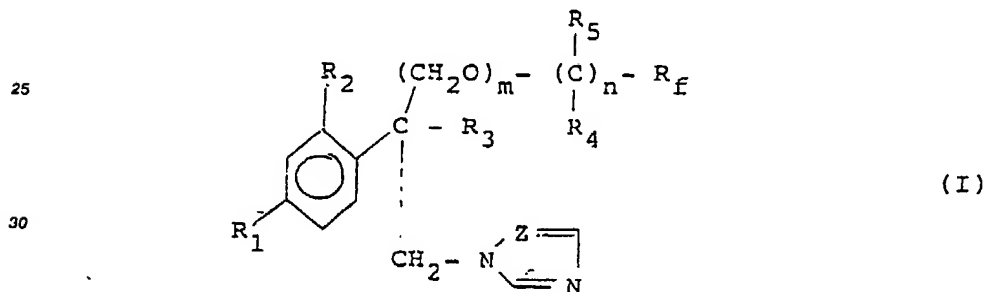
From U.K. Pat. 1,589,852 1-(2-aryl-2-R-ethyl)-1H-1,2,4-triazoles are known, having the general formula:



wherein R is alkyl, cycloalkyl, cycloalkylalkyl, alkenyl, arylalkyl, aryloxyalkyl. By the term "alkyl", the radical of an aliphatic hydrocarbon containing from 1 to 10 carbon atoms is meant.

We have found now a class of 1-(2-aryl-2-R-ethyl)-1H-azoles, wherein the radical R has meanings different from those of the prior art mentioned, endowed with higher fungicidal activity.

An object of the present invention are therefore are compounds, having the general formula:



wherein:

35 $m = 0, 1; n = 0, 1;$

$Z = CH, N;$

R_1 is selected from chlorine, bromine, fluorine, CF_3 , phenyl, C_1 - C_2 -alkoxy, C_1 - C_2 -haloalkoxy, alkylthio such as C_1 - C_2 -alkylthio, haloalkylthio such as C_1 - C_2 -haloalkylthio, wherein the halogen is Cl, Br, F;

R_2 is H, fluorine, chlorine, bromine;

40 R_3 represents H, CH_3 , CN, or also F when $m = 1$ or when $n = 1$ and R_4, R_5 are H;

R_4, R_5 are independently H or F;

R_3 and R_4 , when $m = 0$, can furthermore represent, taken together, a second bond between the two carbon atoms to which they are linked in formula (I);

45 R_1 is selected from the group formed by polyfluoroalkyls, polyfluoroalkenyls and polyfluoroalkynyls containing up to 4 carbon atoms, containing at least 2 F atoms and, optionally, other halogens selected from Cl and Br.

Examples of groups R_1 which can be introduced, according to the present invention, and which are indicated to non-limitative purposes are:

alkyls: $-CHF-CF_3$, $-CHBr-CF_3$, $-CHCl-CF_3$, $-CH_2-CF_3$, $-CF_3-CF_2H$, $-CF_2-CFH-CF_3$;

50 alkenyls: $-CF=CF_2$, $-CF=CF-CF_3$, $-CH=CF-CF_3$, $-CH=CCl-CF_3$, $-CH=CBr-CF_3$, $-CH=C(CF_3)_2$;

alkynyls: $-C\equiv C-CF_3$.

The compounds according to the present invention may have one or more chiral centre(s).

These compounds are generally obtained as racemic mixtures. These mixtures can be separated into the individual enantiomers by methods known from the technical literature.

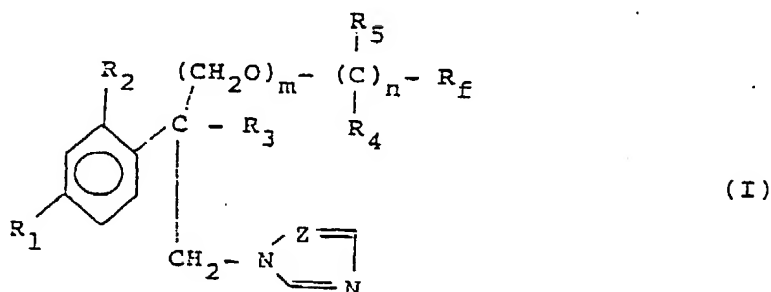
Both the individual enantiomers and the possible diastereoisomers or geometric isomers, generated by more chiral centers or by possible double bonds, are an object of the present invention.

Objects of the present invention are also:

- the salts of the compounds having general formula (I) derived from an inorganic acid, such as a hydrogen halide, e.g., hydriodic, hydrobromic, hydrochloric acid; sulphuric, nitric, thiocyanic and phosphoric acid; or from an organic acid, such as acetic, propanoic, ethanedioic, propanedioic, benzoic, methanesulphonic, 4-methylbenzenesulphonic acid, etc.;
- the metal complexes obtained by the reaction of complexation between the derivatives of type (I) with an organic or inorganic salt of a metal, such as halide, nitrate, sulphate, phosphate of, e.g., copper, manganese, zinc or iron.

Examples of compounds of general formula (I) according to the present invention are reported in Table 1.

Table 1

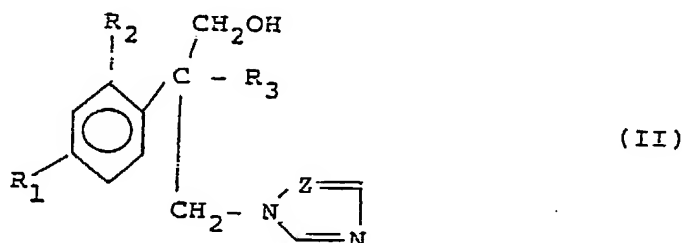


Compound

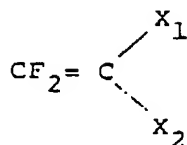
No.	R_1	R_2	R_3	m	n	R_4	R_5	Z	R_F	m.p.
1	Cl	H	H	1	0	-	-	N	$-\text{CF}_2-\text{CF}_2\text{H}$	oil
2	Cl	Cl	H	1	0	-	-	N	$-\text{CF}_2-\text{CF}_2\text{H}$	oil
3	Cl	Cl	H	1	0	-	-	N	$-\text{CF}_2-\text{CFH}-\text{CF}_3$	oil
4	Cl	Cl	H	1	0	-	-	N	$-\text{CF}=\text{CF}-\text{CF}_3$	oil

The compounds having formula (I) can be obtained by applying different processes, according to the value taken by m and n and to the nature of group R_3 . These processes are briefly described hereunder.

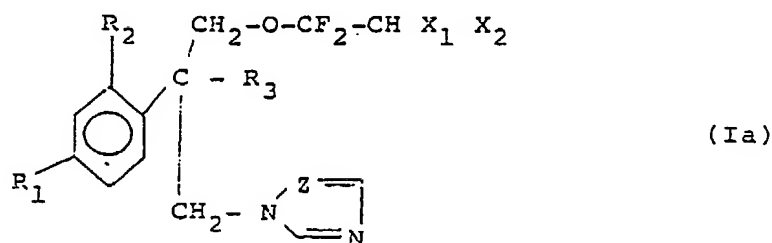
1) A process for the preparation of compounds of formula (I) wherein m is 1 and n is 0, consists in adding an alcohol of formula



wherein R_1 , R_2 , R_3 and Z have the meanings as specified in claim 1, to a 1,1-difluoroolefin having the formula:

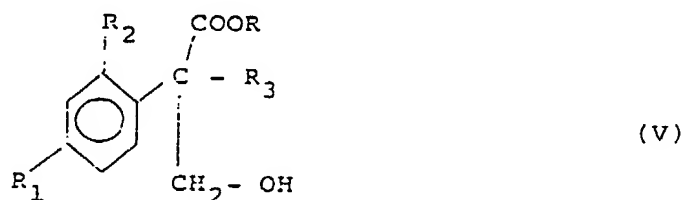


wherein X_1 is Cl, F, CF_3 and X_2 is F, CF_3 , in an aprotic dipolar solvent, such as, e.g., dimethylformamide, or in an alcoholic solvent, such as, e.g., tert.butanol, in the presence of either catalytic or stoichiometric amounts of a strong base, such as, e.g., sodium hydride or potassium tert.butoxide, at temperatures comprised within the range of from 20°C to 100°C, to yield the compounds having formula:

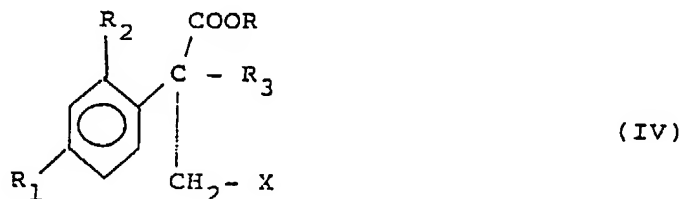


By a dehydrofluorination reaction, which can also take place spontaneously during the above-described reaction, a double bond at the carbon atom in the alpha-position of group R_1 can be introduced. In their turn, the intermediate alcohols of formula (II) can be prepared according to various methods.

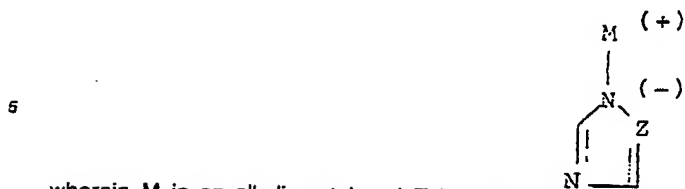
1a) A process for preparing the intermediate alcohols having formula (II) wherein R_1 is H, CH_3 , F, consists in reacting an ester of formula:



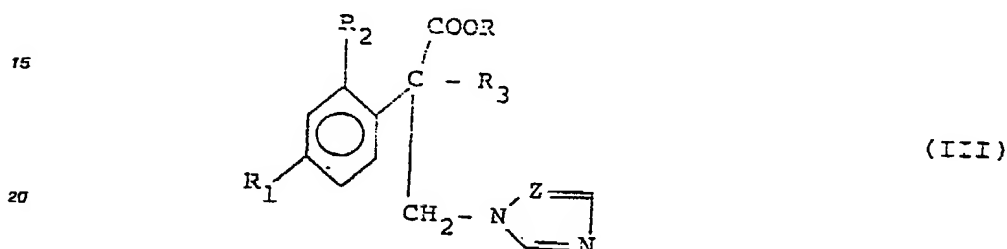
wherein R is either CH_3 or C_2H_5 , known, or obtainable by known methods (Schwenker, Preuntzell, Gassner and Gerber -Chem. Ber., 99 (1966), 2407), with a halogenating agent such as, for example, SOCl_2 , POCl_3 , PCl_5 , PBr_3 , PBr_5 , or a mesylating agent such as, e.g., methanesulphonyl chloride; or with a tosylating agent, such as, e.g., 4-methyl phenylsulphonyl chloride, according to known modalities; in subsequently condensing the intermediate obtained, having formula:



wherein X represents a halogen, a mesyl radical or a tosyl radical, with the alkali-metal salt of an azole of formula:



wherein M is an alkali metal and Z has the meaning given above, in an aprotic dipolar solvent, such as DMSO, DMF or acetone, at temperatures comprised within the range of from 20°C to the reflux temperatures of the solvents; and in finally submitting the so-obtained intermediate compound, having the formula:

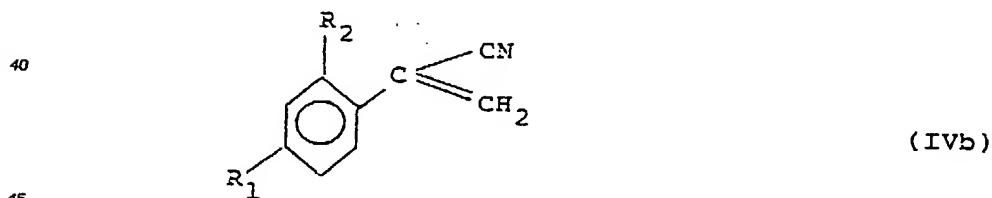


to reduction, by means of the use of such metal hydrides as, e.g., LiAlH₄, in etheric solvents, such as ethyl ether or THF.

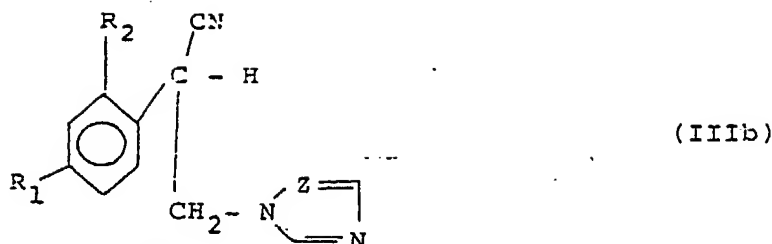
25 The intermediate esters of formula (III) wherein R₁ is H, can be prepared, according to an alternative route, by means of the addition of an azole of formula:



35 to a known compound of formula:



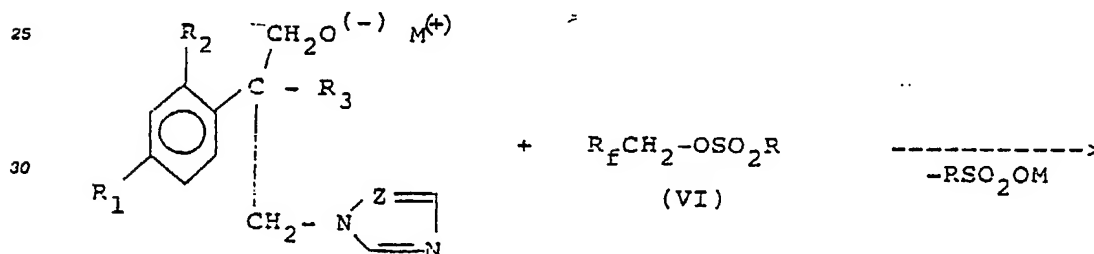
(known, for example, from Colonge, Dreux et Regeand, Bull. Soc. Chim. Fr., 1959, 1244), in apolar solvents such as, e.g., toluene or benzene, in the presence of catalytic amounts of an organic base such as, e.g., triethylamine, at boiling temperature, or in an alcoholic solvent, in the presence of either catalytic or stoichiometric amounts of an alkali-metal base, such as, e.g., NaOH or KOH, at the reflux temperature of the solvent, and in subsequently converting -CN group of the intermediates obtained, of formula:



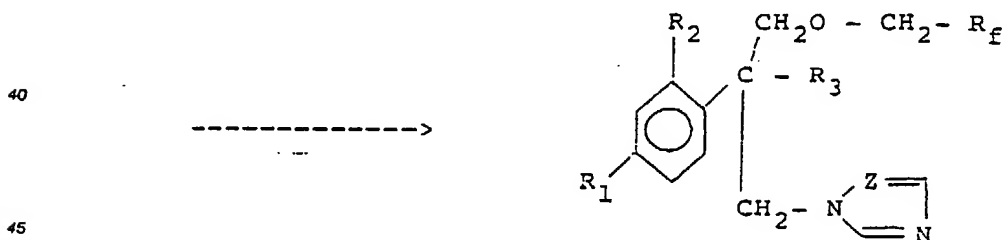
10 into a -COOR group, by treatment with mineral acids, such as, e.g., gaseous HCl, H₂SO₄, in alcoholic solvents, at temperatures comprised within the range of from 0°C to the boiling temperature of the solvent. By so operating, the esters (III) wherein R₃ = H can be converted by reduction, as indicated above, into the alcohols (II), wherein R₃ = H.

15 1b) Another route for the preparation of the intermediate alcohols having formula (II) wherein R₃ is -CN consists in reacting the above intermediate of formula (IIIb) with paraformaldehyde or trioxymethylene, in aprotic dipolar solvent, such as, e.g., DMSO or DMF, in the presence of catalytic amounts of a strong base such as, e.g., sodium methoxide or sodium ethoxide, KOH, NaOH or sodium hydride, at temperatures comprised between room temperature and 100°C.

20 2) The compounds of formula (I), wherein $\underline{m} = 1$, $\underline{n} = 1$, R₄ = R₅ = H, can be obtained by the reaction of the alkali-metal salt of a compound of formula (II), obtained by the reaction between a compound of formula (II) and a strong base such as, e.g., sodium hydride, with a fluorinated sulphonic ester having formula (VI), according to the reaction scheme:



35 alkali-metal salt of (II)



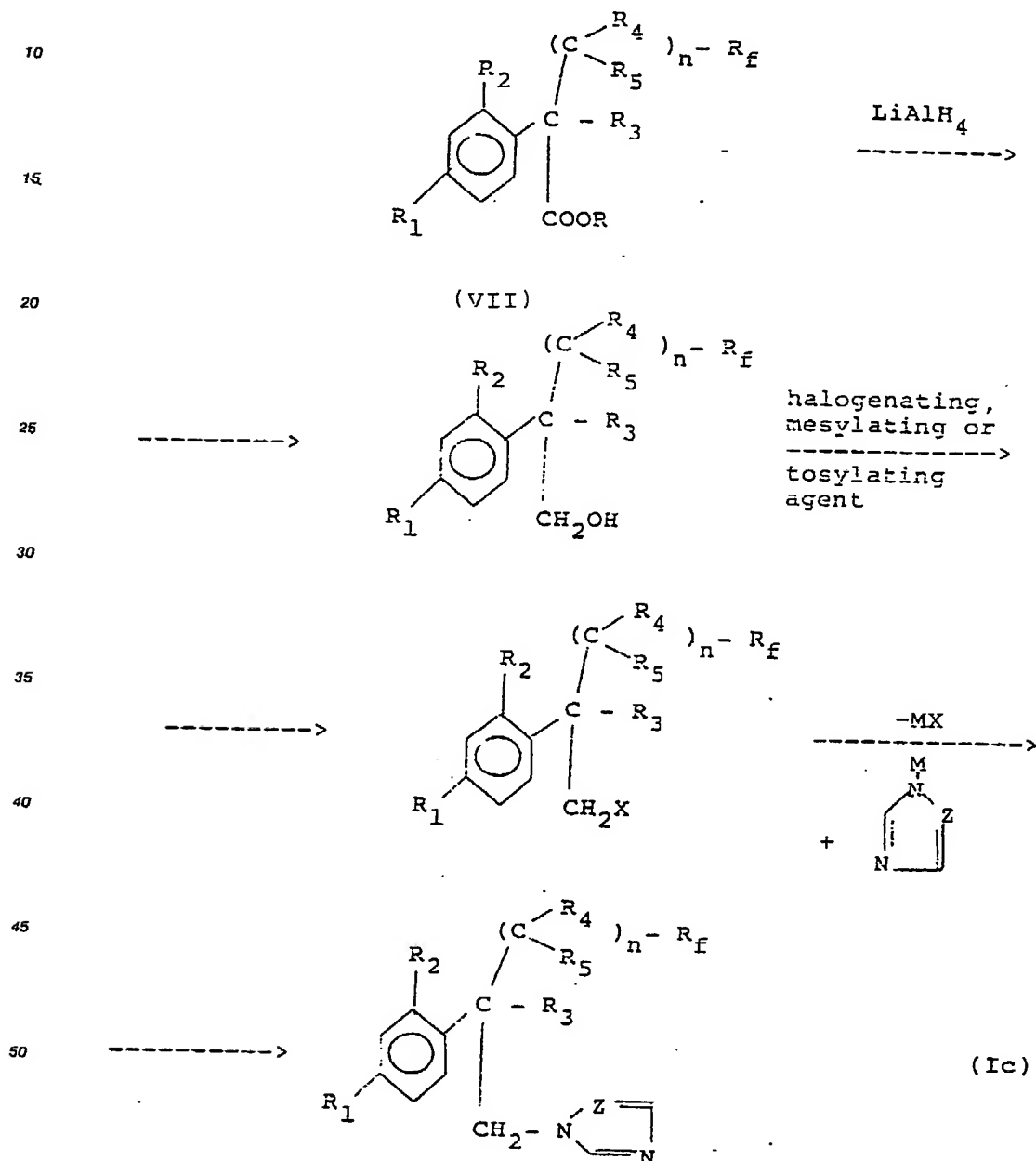
(Ib)

50 wherein R is CH₃, p-tolyl, CF₃.

The same compounds of formula (Ib) can be obtained also by the reaction of a sulphonic ester of compound (II) with the alkali-metal salt of the fluorinated alcohol R_fCH₂OH.

55 Examples of R_f groups in compounds (VI) and in R_fCH₂OH alcohols are: -CF₃-CHF₂, -CF₃-CHF₂CF₃, -CF₃, -C₂F₅, -C₃F₇, -C₄F₉. From compounds having formula (Ib) wherein in the group R_f at least a hydrogen atom is present, introducing a double bond into the same group is possible by dehydrofluorination reaction.

3) when $\underline{m} = 0$; $\underline{n} = 0, 1$; $R_4 = H, Me, F$, the compounds having formula (I) can be prepared by starting from the carboxylic esters of formula (VII), by reduction by methods per se known, for example, by using $LiAlH_4$, followed by the conversion of the alcoholic function so obtained into a leaving group (e.g., mesylate, tosylate, halogen) and finally by the condensation of the reactive intermediate resulting by such a conversion with an alkali-metal salt of the proper azole, by modalities analogous to those described for the preparation process (1.a) according to the reaction schemes:



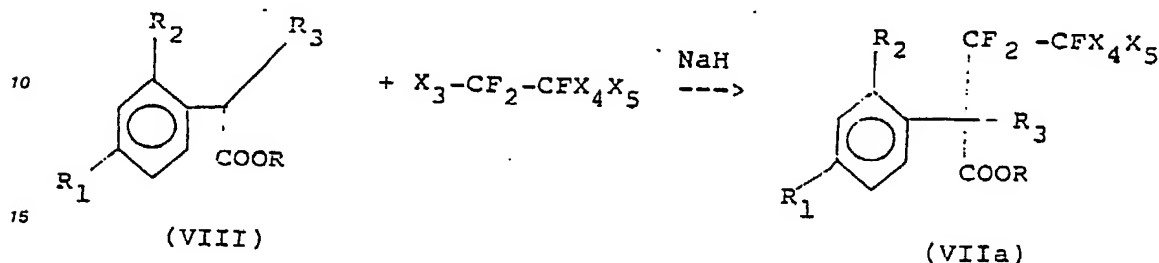
In the above formulae, R_1, R_2, R_4, R_5, R_f and n have the meanings given for the compound of formula (I); R_3 is H, CH_3, F ; R is CH_3, C_2H_5 ; M is an alkali-metal; X = halogen, mesyl, tosyl.

The intermediate esters having formula (VII) can be prepared in their turn by various methods hereunder briefly described.

3a) Condensation of the alkali-metal salt of an arylacetic ester of type (VIII), prepared according to known methods (e.g., from Middleton, Bingham, J.A.C.S. 1980 (102) (14), 4845-6), with a fluoroalkane:

5 $X_3-CF_2-CFX_4X_5$,

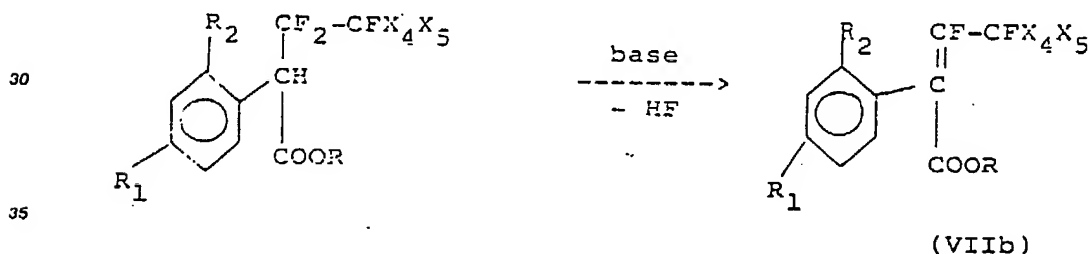
according to the reaction scheme:



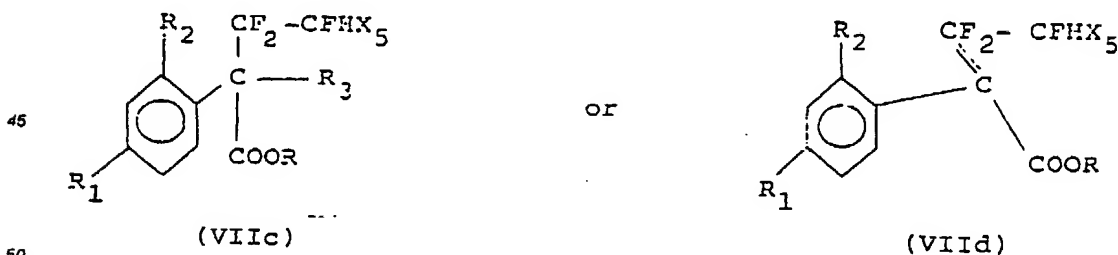
wherein $R_3 = H, CH_3$; $R = CH_3, C_2H_5$; X_3 is bromine or iodine, X_4 is bromine, iodine and X_5 can be fluorine or a C_1-C_3 -perfluoroalkyl.

20 The reaction can be carried out in dipolar aprotic solvent such as DMF, DMSO, in an ether solvent, such as ethyl ether, THF, dioxane, at temperatures comprised within the range of from room temperature to the reflux temperature of the solvent used.

25 3b) Dehydrofluorination of esters (VIIa) wherein $R_3 = H$, by strong bases in aprotic dipolar solvents, at temperatures comprised within the range of from room temperature to the reflux temperature, or spontaneously during the same reaction of preparation of compounds (VIIa), according to the scheme:



3c,d) By reduction of compounds (VIIa) or (VIIb) according to known methods, by using, e.g., $NaBH_4$, Zn and acids, Na amalgam, hydrogen and catalysts, compounds of type:

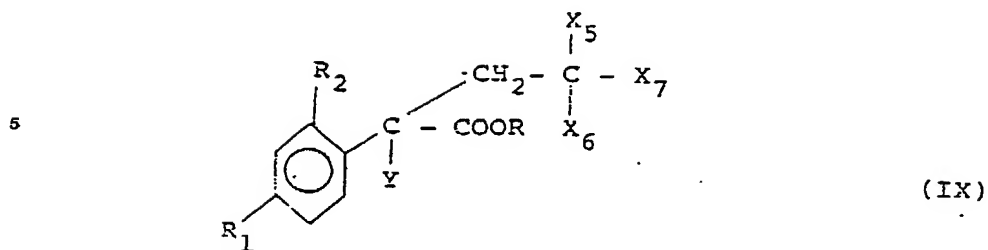


can be obtained.

From compounds of type (VIIc), wherein $R_3 \neq H$, introducing a double bond in the fluorinated chain, by a dehydrofluorination reaction, is possible.

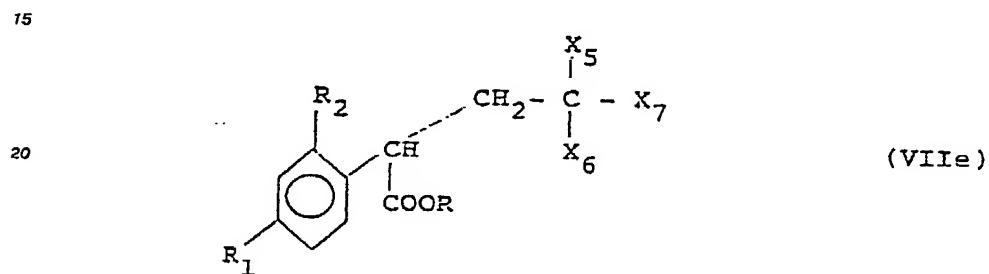
3e,f,g) Reduction of the compounds of formula:

55

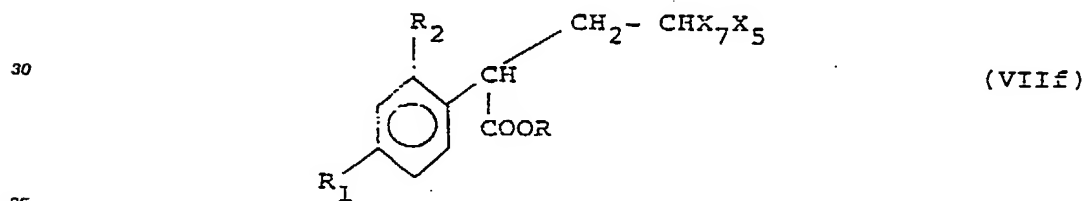


10 wherein X_7 , X_6 equal to or different from each other, are F, Cl, Br; X_5 is either F or a C_1 - C_2 perfluoroalkyl; Y is Br, I or also chlorine when X_7 and X_6 are F, Cl.

This reduction is carried out by methods known in the technical literature and, according to the selected experimental conditions and to the reactant used, can lead to compounds of formula:

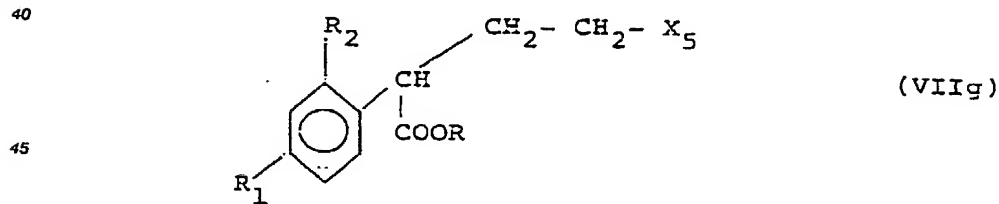


25 or of formula



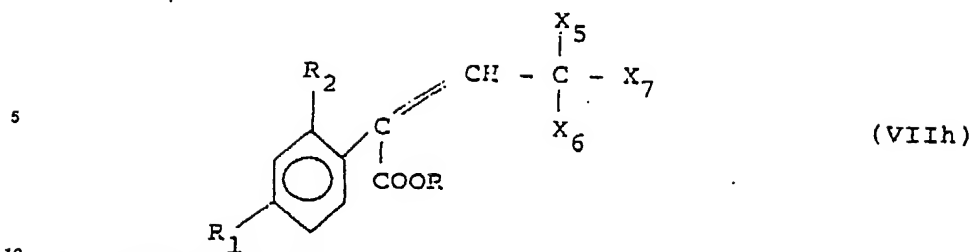
(when X_6 is \neq F),

or of formula

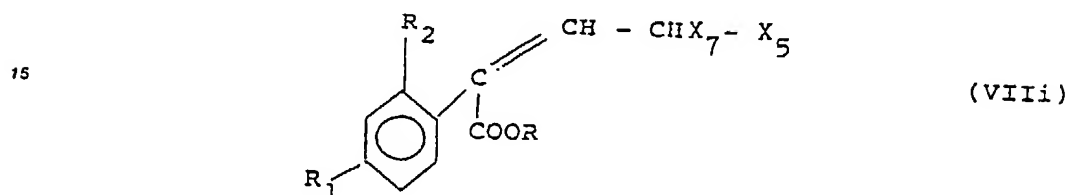


when X_6 , X_7 are different from F.

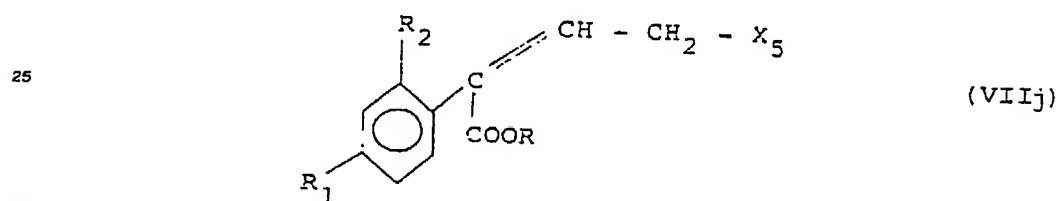
50 3h,i,j) By dehydrohalogenation by the known methodologies seen above, by starting from compounds of formula (IX), compounds of type



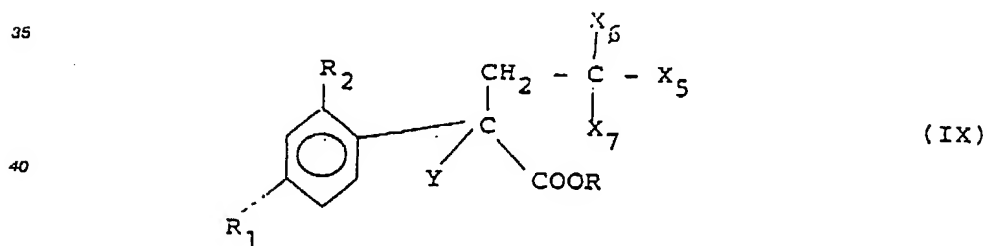
10 can be obtained, from which, by reduction of the reactive halogens, arriving is possible to compounds of type



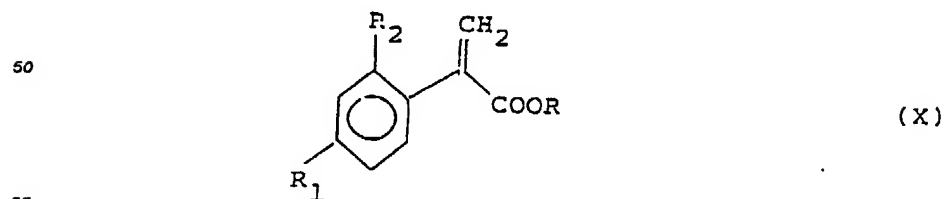
20 and



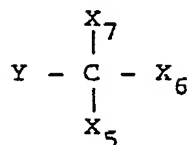
30 when X₆ and, respectively, X₇, are different from F. The compounds of type (IX) of formula



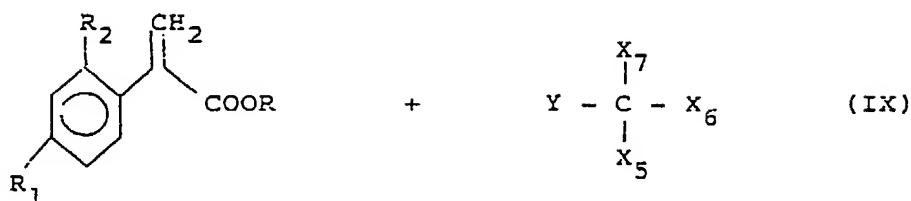
40 are prepared in their turn by the addition reaction between the compounds known (e.g., from Schwenker, Preuntzell, Gassner and Gerber, Chem. Ber., 99 (1966), 2407), of formula:



55 and a polyfluoroalkane of general formula

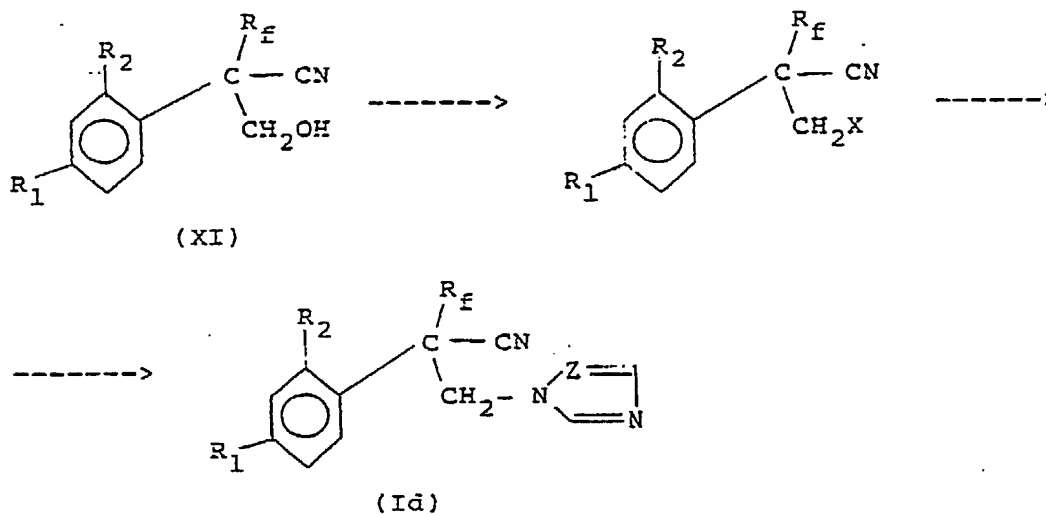


according to the reaction scheme:

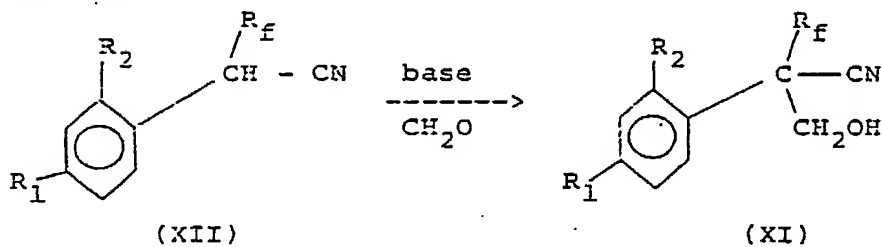


The reaction is generally carried out in alcoholic solvents, such as tert.butanol, or in the absence of solvents, at temperatures comprised within the range of from room temperature to 140°C, with known catalysts, such as benzoylperoxide or tert.butylperoxide, copper(I) chloride + ethanolamine or FeCl₃ or azobisisobutyronitrile and U.V. light.

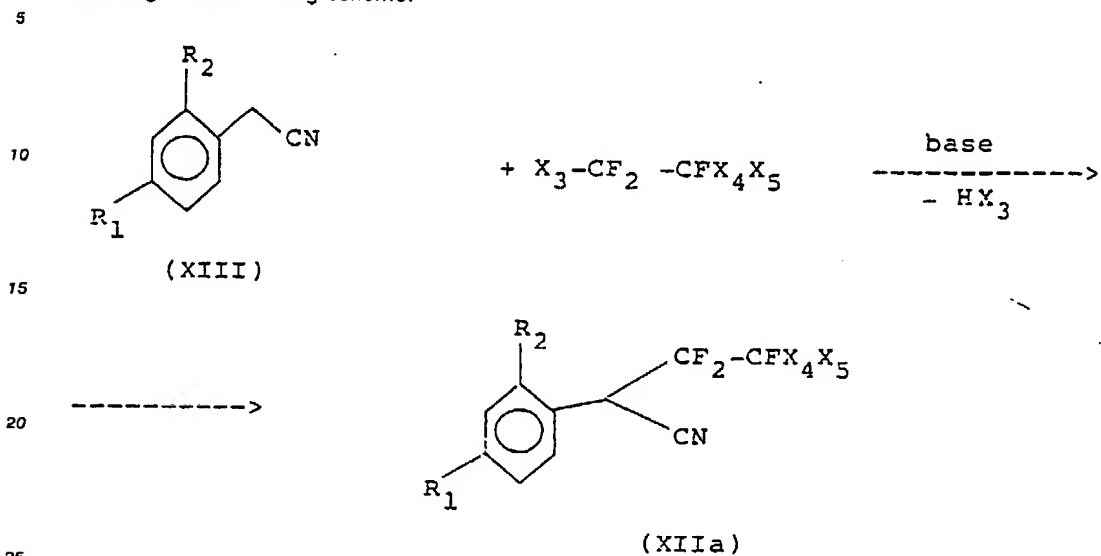
4) The compounds of general formula (I) wherein $\underline{m} = 0$, $\underline{n} = 0$ and $\text{R}_1 = -\text{CN}$ can be prepared by the conversion of the alcohols of type (XI), through the reaction route analogous to that of process (3).



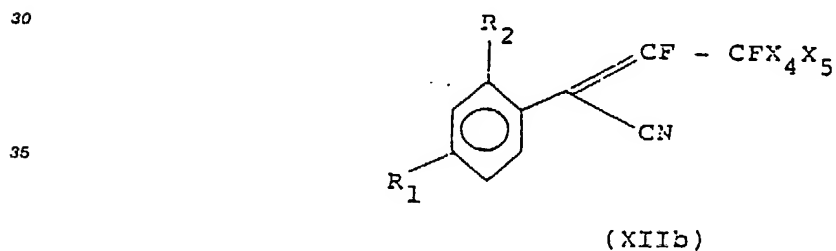
The intermediate alcohols of formula (XI) are prepared in their turn by starting from compounds of type - (XII) by the introduction of a methylol group, under conditions analogous to those illustrated in the second reaction of process (1b):



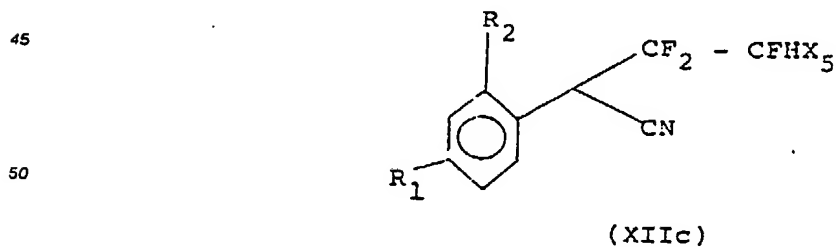
Compounds (XII) can be prepared by starting from known benzyl nitriles of type (XIII), by condensation with a fluoroalkane of type $X_3-CF_2-CFX_4X_5$, under conditions analogous to those illustrated in preparation 3a) according to the following scheme:



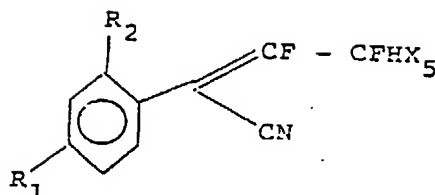
From compounds (XIIa) obtaining is possible, by dehydrofluorination reaction, unsaturated compounds of formula:



Finally, by starting from compounds XIIa and XIIb, by reduction according to methods per se known, obtaining is possible compounds of type



and respectively



(XII d)

The compounds having general formula (I) are endowed with fungicidal activity particularly high against phytopathogenous fungi which attack cultivations of cereals, of Cucurbitaceae, of grapevine and of fruit-trees.

Examples of plant diseases which can be fought by the compounds of the present invention are the following:

- Erysiphe graminis on cereals;
 - Sphaerotheca fuliginea of Cucurbitaceae (e.g., of cucumber)
 - Puccinia on cereals
 - Septoria on cereals
 - Helminthosporium on cereals
 - Rhynchosporium on cereals
 - Podosphaera leucotricha on apple-tree
 - Uncinula necator on grapevine
 - Venturia inaequalis on apple-tree
 - Piricularia oryzae on rice
 - Botrytis cinerea
 - Fusarium on cereals
- and still further diseases.

The compounds having formula (I) are furthermore endowed with other positive characteristics, such as a fungicidal activity both curative and preventive in character, as well as a complete tolerability by the plants to be protected against the fungal infection.

Besides the high fungicidal activity with preventive and curative application, the compounds of formula (I) are characterized by systemic properties.

These properties allow the products to enter into the vascular systems of plants, and act in sites (e.g., leaves) even very remote from those to which they are applied (e.g., roots).

For the practical uses in agriculture, having available fungicidal compositions containing one or more compounds of formula (I) as the active substance is often useful.

The application of these composition can be carried out on any part of the plants, e.g., on leaves, stems, limbs and roots, or on the same seeds, before the sowing, or also on the soil the plant is growing on. Compositions can be used, which have the form of dry powders, wettable powders, emulsifiable concentrates, pastes, granulates, solutions, suspensions, and so forth: the selection of the type of composition shall depend on the specific use. The compositions are prepared in known way, e.g., by diluting or dissolving the active substance with a solvent means and/or a solid diluent, optionally in the presence of surface-active agents. As solids diluents, or carriers, used can be: silica, kaolin, bentonite, talc, fossil flour, dolomite, calcium carbonate, magnesia, gypsum, clays, synthetic silicates, attapulgite, sepiolite. As liquid diluents, besides of course water, various types of solvents can be used such as, e.g., aromatic solvents (benzene, xylenes or mixtures of alkylbenzenes), chloroaromatic solvents (chlorobenzene), paraffins (petroleum fractions), alcohols (methanol, propanol, butanol), amines, amides (dimethylformamide), ketones (cyclohexanone, acetophenone, isophorone, ethyl-amyli-ketone), esters (isobutyl acetate). As surfactants: sodium, calcium or triethanolamine salts of alkylsulphates, alkylsulphonates, alkyl-arylsulphonates, polyethoxylated alkylphenols, fatty alcohols condensed with ethylene oxide, polyoxyethylated fatty acids, polyoxyethylated sorbitol esters, polyoxyethylated fats, lignine sulphonates can be used. The compositions can also contain special additives for particular purposes, e.g., such adhesive-properties-conferring agents as gum arabic, polyvinyl alcohol, polyvinylpyrrolidone.

If desired, to the compositions of the present invention also other compatible active substances as fungicides, phytomedicines, phyto regulators, herbicides, insecticides, fertilizers can be added.

The concentration of active substance in the said compositions can vary within a wide range, according to the active compound, to the cultivation, to the pathogen agent, to the environmental conditions and to the type of formulation adopted. In general, the concentration of active substance varies from 0.1 to 95%, preferably from 0.5 to 90% by weight.

5 The following examples illustrate the invention.

EXAMPLE 1

10 Preparation of 1-(1H-1,2,4-triazol-1-yl)-2-(4-chlorophenyl)-3-(1,1,2,2-tetrafluoroethoxy)-propane (Compound No. 1)

An amount of 0.4 g of NaH in oil suspension at 55% is dispersed in 10 ml of anhydrous DMF under nitrogen atmosphere. At room temperature, 2.4 g of 2-(4-chlorophenyl)-3-(1H-1,2,4-triazol-1-yl)-propanol
15 dissolved in 10 ml of anhydrous DMF is added. When the reaction is complete (over a time of about 30 minutes), the reaction mixture is cooled to 0°C, and tetrafluoroethylene is added, the flow rate thereof being so adjusted that the reaction temperature does not exceed 30°C.

At the end of heat evolution, the temperature is allowed to rise again to room temperature.

The reaction mixture is poured into water, and is extracted with dichloromethane. The organic extract is
20 washed with water, dried over Na₂SO₄ and evaporated under vacuum. The residual oil (2.9 g) is purified over silica gel, using 8:2 n-hexane + diethylether as the eluent. 0.5 g of colourless viscous oil is obtained, which is characterized as having the structure indicated at example title on the basis of the following spectroscopic data.

-I.R. (ν , cm⁻¹): 680, 1120, 1210, 1275, 1500.

25 -¹H-N.M.R. (200 MHz) in CDCl₃, δ = 3.56 (quint., 1 H) --

4.11 (m, 2 H)

4.42 (2dd, 2 H)

5.667 (tt, 1 H)

6.945-7.013; 7.181-7.249 (2 m, 4 H)

30 7.681 (s, 1 H)

7.853 (s, 1 H)

EXAMPLE 2

35 Preparation of 2-(4-chlorophenyl)-3-(1H-1,2,4-triazol-1-yl)propanol

1.3 g of LiAlH₄ is suspended in 170 ml of anhydrous diethyl ether under N₂ atmosphere. Within one hour, 8 g of methyl α -(1H-1,2,4-triazol-1-ylmethyl)-4-chlorophenylacetate is introduced. The reaction is
40 exothermic, and proceeds with solvent reflux. At the end of heat evolution, 10 ml of methanol in 50 ml of diethyl ether is added, to destroy the excess of hydride.

The reaction mixture is filtered over celite and from the filtrate, after concentration, 6.8 g of solid product is obtained which is washed with a few ml of n-hexane-acetone mixture, up to obtain 5.3 g of a white solid (m.p. 137-9°C) having the structure indicated at Example title.

45 -I.R. (ν , cm⁻¹) in oil: 830, 1018, 1065, 1140, 1284, 3115, 3210.

EXAMPLE 3

50 Preparation of methyl α -(1H-1,2,4-triazol-1-yl)-4-chlorophenylacetate

A suspension of 3.2 g of 1,2,4-triazole and 8.3 g of K₂CO₃ in 300 ml of anhydrous acetone is refluxed over 1 hour. After cooling to 10°C, 14 g of methyl α -(methanesulphonyloxymethyl)-4-chlorophenyl-acetate is added. The temperature is then allowed to spontaneously rise to room temperature, and the reaction
55 mixture is stirred for one hour, is filtered over fritted glass and the filtrate is concentrated under vacuum, 13 g being obtained of raw solid product, which is suspended with 10 ml of 1:1 n-hexane + ethanol mixture.

10.8 g is thus obtained of white solid (m.p. 92-3°C), having the structure indicated at Example title.
-I.R. (ν , cm^{-1}) in oil: 840, 1019, 1092, 1142, 1225, 1743.

5 EXAMPLE 4

Preparation of methyl α -(methanesulphonyloxymethyl)-4-chlorophenyl-acetate

To a solution of 5 g of methyl α -(hydroxymethyl)-4-chlorophenylacetate and 3.5 g of methanesulphonyl chloride in 30 ml of anhydrous diethyl ether, cooled at 0°C, a solution of 2.6 g of triethylamine in 10 ml of anhydrous diethyl ether is added dropwise. The temperature is allowed to rise again to room temperature, the reaction mixture is poured into water and is extracted with diethyl ether. The ether solution, washed with water, and dried over Na_2SO_4 , is concentrated under vacuum, to yield 7.2 g of raw product. By crystallization thereof from 5 ml of ethanol, 5.4 g is obtained of white solid product (m.p. 77-8°C), having the structure indicated at Example title.

-I.R. (ν , cm^{-1}): 1100, 1180, 1210, 1492, 1725.

EXAMPLE 5

20 Preparation of 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-dichlorophenyl)-3-(1,1,2,2-tetrafluoroethoxy)-propane (Compound No. 2)

This compound is prepared by a process similar to that disclosed at Example 1, by starting from 2-(2,4-dichlorophenyl)-3-(1H-1,2,4-triazol-1-yl)-propanol, prepared in its turn by a process similar to that described at Examples 4, 3 and 2.

Compound No. 2 is isolated as colourless viscous oil and is characterized by the following spectroscopic data.

-I.R. (ν , cm^{-1}): 683, 1120, 1210, 1278, 1478, 1505.

30 $^1\text{H-N.M.R.}$ (60 MHz) in CCl_4 , δ = 4 -4.7 (m, 5 H)

5.72 (tt, 1 H)

7 -7.6 (m, 3 H)

7.74 (s, 1 H)

7.8 (s, 1 H)

EXAMPLE 6

Preparation of methyl 2-(4-chlorophenyl)-4-bromo-3,4,5,5,5-pentafluoropent-2-enoate

40 0.8 g of sodium hydride in oil suspension at 55% is dispersed in 10 ml of anhydrous DMF under N_2 atmosphere.

At room temperature, 3 g of methyl 4-chlorophenylacetate dissolved in 10 ml of anhydrous DMF is added. When the reaction is complete (over a time of about 30 minutes), the reaction mixture is added dropwise under N_2 atmosphere, to a solution of 5 g of 1,2-dibromo-1,1,2,3,3,3-hexafluoropropane in 10 ml of anhydrous DMF. After 1 hour at room temperature, the reaction mixture is poured into water, and is extracted with dichloromethane. The organic extract is washed with water up to neutral pH, dried over Na_2SO_4 and evaporated under vacuum to yield 4 g of raw product. This is purified by chromatography over silica gel, using 95:5 n-hexane + diethylether as the eluent. 1.5 g of slightly yellow liquid is obtained, having the structure indicated at Example title, according to the following spectroscopic data:

-I.R. (ν , cm^{-1}): 900, 1125, 1220, 1282, 1492, 1594, 1664, 1740.

$^1\text{H-N.M.R.}$ (60 MHz) in CCl_4 , δ = 3.82 (s, 3 H)

7.43 (s broad, 4 H)

55 EXAMPLE 7

Preparation of 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-dichlorophenyl)-3-(1,1,2,3,3,3-hexafluoropropoxy)-propane (Compound No. 3) and of 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-dichlorophenyl)-3-(1,1,2,3,3,3-hexafluoropropenoxy)-propane (Compound No. 4)

5 The above mentioned compounds have been obtained as a mixture, by starting from 2-(2,4-dichlorophenyl)-3-(1H-1,2,4-triazol-1-yl)propanol and hexafluoropropene, and by a process analogous to that disclosed at Example 1.

The compounds have been isolated as colourless viscous oils, and characterized by the following spectroscopic data:

10

Compound No. 3:

-I.R. (ν , cm^{-1}): 1760, 1590, 1510, 1478, 1280, 1190, 1040.

15 $^1\text{H-N.M.R.}$ (60 MHz) in CCl_4 , $\delta = 7.75$ (s, 1 H)

7.7 (s, 1 H)

7.50-6.80 (m, 3 H)

5.25 (m, 0.5)

4.40-4.45 (d, 2 H)

20 4.20 (s broad, 2 H)

4.7-3.8 (m, 1.5 H)

Compound No. 4:

25

-The I.R. spectrum is equal to that of Compound No. 3, with the exception of the band at 1760 cm^{-1} , which is absent.

$^1\text{H-N.M.R.}$ (60 MHz) in CCl_4 , $\delta = 7.75$ (s, 1 H)

7.70 (s, 1 H)

30 7.50-6.80 (m, 3 H)

4.40-4.45 (d, 2 H)

4.20 (s broad, 2 H)

4.55-3.80 (m, 1 H).

35

Preparation of 1-(1,2,4-triazol-1-yl)-2-(4-chlorophenyl)-2-(1,1,2,2-tetrafluoroethoxy)-methyl-propane (Compound No.5).

40 An amount of 0,1 g of potassium tert.-butoxide is added, under nitrogen atmosphere at -10°C , to 1,9 g of 2-(4-chlorophenyl)-2-methyl-3-(1,2,4-triazol-1-yl)-1-hydroxy-propane dissolved in 6,5 ml of anhydrous THF, 13 ml of anhydrous DMSO, 13 ml of anhydrous tert.-butanol.

The apparatus is then put under vacuum and tetrafluoroethylene is introduced by maintaining the reaction mass under this gas atmosphere over a time of a night, at room temperature.

45 The reaction mixture then is poured into water, and is extracted with ethyl acetate. The extract is washed with water, dried over Na_2SO_4 and evaporated; the raw product obtained is purified by chromatography over silica gel, using n-hexane-ethyl acetate 1:1 as eluent. 1 g of an oil is isolated having the structure of Compound No.5, according to the following spectroscopic data:

-I.R. (cm^{-1}) 1580, 1280, 1210, 1120.

$^1\text{H-NMR.}$ (60 MHz) TMS in CDCl_3 , $\delta = 1,30$ (s, 3 H),

50 4,00 (s broad, 2 H);

4,25 (s broad, 2 H);

5,55 (tt, 1 H);

6,80-7,20 (m, 4 H);

7,35 (s, 1 H);

55 7,55 (s, 1 H).

Likewise to Compound No.5, 1-(1,2,4-triazol-1-yl)-2-(2,4-dichlorophenyl)-2-(1,1,2,2-tetrafluoroethoxy)-methyl-propane is prepared.

The compound is characterized by the following spectroscopic data.

¹H-NMR. (60 MHz) TMS in CDCl₃.

δ = 1,35 (s, 3 H);

3,90 (s broad, 2 H);

5: 4,05 (s broad, 2 H);

5,50 (tt, 1 H);

6,80-7,20 (m, 3 H);

7,45 (s, 1 H);

7,60 (s, 1 H).

10

EXAMPLE 9

Determination of the fungicidal activity against cucumber oidium (*Sphaerotheca fuliginea*(schlech) Salmon)

15 Preventive activity:

Cucumber plants, cv. Marketer, grown in pot in conditioned environment, have been sprinkled on the lower faces of their leaves with the products under test in water-acetonic solution at 20% (v/v) of acetone. The plants have been subsequently kept in conditioned environment for 1 day, and have been then
20 sprinkled on the upper face of the leaves with an aqueous suspension of conidia of *Sphaerotheca fuliginea* - (200,000 conidia per ml). The plants have been then placed again in conditioned environment.

At the end of the incubation time of the fungus (8 days), the severity of the infection has been evaluated, and it has been given a rating based on an evaluation scale going from 100 (= healthy plant) to 0 (= completely infect plant).

25

Curative activity:

Plants of cucumber cv. Marketer, grown in pot in conditioned environment, have been sprayed on the
30 upper face of the leaves with an aqueous solution of conidia of *Sphaerotheca fuliginea* (200,000 conidia per ml). After 24 hours from the infection, the plants have been treated with the products under test in water-acetonic solution at 20% (v/v of acetone), by spraying of both the faces of their leaves.

At the end of the incubation time of the fungus (8 days), during which the plants have been preserved in suitably conditioned environment, the severity of the infection has been evaluated, and it has been given
35 a rating based on an evaluation scale going from 100 (= healthy plant) to 0 (= completely infect plant).

The results are reported in Table 2.

EXAMPLE 10

40

Determination of the fungicidal activity against the oidium of wheat (*Erysiphe graminis* D.C.)

Preventive activity:

45 The leaves of wheat, cv. Irnerio, grown in pot in conditioned environment, have been treated by sprinkling of both their faces with the products under test in water-acetonic solution at 20% (v/v) of acetone.

After one day of permanence in conditioned environment, the plants have been sprinkled on both the faces of their leaves with an aqueous suspension of *Erysiphe graminis* (200,000 conidia per ml). After 24 hours of permanence in a humidity-saturated environment, at 21°C, the plants have been kept in a
50 conditioned environment for the incubation of the fungus.

At the end of said incubation period (12 days), the severity of the infection has been evaluated visually, and it has been given a rating based on an evaluation scale going from 100 (= healthy plant) to 0 (= completely infect plant).

55

Curative activity:

The leaves of wheat cv. Irnerio, grown in pot in conditioned environment, have been sprayed on both their faces with an aqueous suspension of Erysiphe graminis (200,000 conidia per ml). After 24 hours of permanence in humidity-saturated environment, at 21°C, the leaves have been treated with the products under test in water-acetonic solution at 20% (v/v of acetone), by spraying of both their faces.

At the end of the incubation time (12 days), the severity of the infection has been visually evaluated, and it has been given a rating based on an evaluation scale going from 100 (= healthy plant) to 0 (= completely infect plant).

The results are reported in Table 2.

EXAMPLE 11

Determination of the fungicidal activity against the linear blight of wheat (*Puccinia graminis* Pers.)

Preventive activity:

The leaves of wheat, cv. Irnerio, grown in pot in conditioned environment, have been treated by sprinkling of both their faces with the products under test in water-acetonic solution at 20% (v/v) of acetone. After one day of permanence in environment conditioned at 23°C and 70% R.H., the plants have been sprinkled on both the faces of their leaves with a mixture of spores of Puccinia graminis in talc (100 mg of spores per 5 g of talc). After 48 hours of permanence in a humidity-saturated environment, at 21°C, the plants have been kept in a conditioned environment for the incubation of the fungus.

At the end of said incubation period (14 days), the severity of the infection has been evaluated visually, and it has been given a rating based on an evaluation scale going from 100 (= healthy plant) to 0 (= completely infect plant).

Curative activity:

The leaves of wheat cv. Irnerio, grown in pot in conditioned environment, have been sprayed on both their faces with a mixture of spores of Puccinia graminis in talc (100 mg of spores/5 g of talc); after 48 hours of permanence in humidity-saturated environment, at 21°C, the leaves have been treated with the products under test in water-acetonic solution at 20% (v/v of acetone), by spraying of both their faces.

At the end of incubation time (14 days), the severity of the infection has been visually evaluated, and it has been given a rating based on an evaluation scale going from 100 (= healthy plant) to 0 (= completely infect plant).

The results are reported in Table 2.

TABLE 2

Compound No.	Dosis g/l	Sphaerotheca fuli- ginea/cucumber		Erysiphe graminis trit./wheat		Puccinia graminis/ wheat	
		Preventive Activity	Curative Activity	Preventive Activity	Curative Activity	Preventive Activity	Curative Activity
1	0.5	100	100	100	100	100	100
	0.25	100	100	100	100	100	100
	0.125	100	100	100	100	70	100
2	0.5	100	100	100	100	100	100
	0.25	100	100	100	100	100	100
	0.125	100	100	100	100	100	100
Ref.*	0.5	100		100		50	
	0.25	100		100		0	
	0.125	100		100		0	

Ref* corresponds to the reference compound 1-[2-(2,4-dichlorophenyl)pentyl]-1H-1,2,4-triazole, known as Penconazole (Topas), of U.K.Pat. 1,589,652.

EXAMPLE 12

Determination of the Foliar Systemic Activity on Wheat Oidium (*Erysiphe graminis* d.c.)

The leaves of wheat, cv. Irnerio, grown in pot in conditioned environment, have been treated by sprinkling of both their faces with the products under test in water-acetonic solution at 20% (v/v) of acetone. Five days after the treatment, the leaves treated, and the new leaves emitted in the meantime, have been sprinkled on both their faces with an aqueous suspension of *Erysiphe graminis* (200.000 conidia per ccm). After 24 hours of permanence in a humidity-saturated environment, at 21°C, the plants have been kept in a conditioned environment for the incubation of the fungus.

At the end of said incubation period (12 days), the severity of the infection has been evaluated visually, and it has been given a rating based on an evaluation scale going from 100 (= healthy plant) to 0 (= completely infect plant).

The results shown in Table 3 have been obtained.

TABLE 3Foliar Systemic Activity on Erysiphe graminis

<u>Compound No.</u>	<u>Dosis, g/l</u>	<u>Treated Leaves</u>	<u>Untreated Leaves</u>
2	0.0018	100	100
penconazole	0.0018	42	14

-propiconazole = 1-[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl-methyl]-1H-1,2,4-triazole.
 -triadimefon = 1-(4-chlorophenoxy)-3,3-dimethyl-1-[(1H-1,2,4-triazol-1-yl)-butanone].

EXAMPLE 13

Determination of the Foliar Systemic Activity on linear blight of Wheat (*Puccinia graminis* Pers.)

The leaves of wheat, cv. Irnerio, grown in pot in conditioned environment, have been treated by sprinkling of both their faces with the products under test in water-acetonic solution at 20% (v/v) of acetone. Five day after the treatment, the leaves treated, and the new leaves emitted in the meantime, have been sprinkled on both their faces with a mixture of spores of *Puccinia graminis* in talc (100 mg of spores/5 g of talc). After 48 hours of permanence in a humidity-saturated environment, at 21°C, the plants have been kept in a conditioned environment for the incubation of the fungus.

At the end of said incubation period (14 days), the severity of the infection has been evaluated visually, and it has been given a rating based on an evaluation scale ranging from 100 (= healthy plant) to 0 (= completely infect plant).

The results shown in Table 4 have been obtained.

TABLE 4Foliar Systemic Activity on Puccinia graminis Pers.

<u>Compound No.</u>	<u>Dosis, g/l</u>	<u>Treated Leaves</u>	<u>Untreated Leaves</u>
2	0.5	100	100
penconazole	0.5	20	0

EXAMPLE 14

Determination of the fungicidal activity on brown-spotting of apple-tree (*Venturia inaequalis* (cke) Wint)

Preventive activity:

The leaves of apple-tree, cv. Starking, grown in pot in greenhouse, have been treated by sprinkling of both their faces with the products under test in water-acetonic solution at 20% (v/v) of acetone. After one day of permanence in environment conditioned at 20°C and 70% R.H., the plants have been sprinkled on both the faces of their leaves with an aqueous suspension of conidia of *Venturia inaequalis* (200,000 conidia per ccm). After 2 days of permanence in a humidity-saturated environment, at 21°C, the plants have been preserved in a conditioned environment for the incubation of the fungus.

At the end of said incubation period (14 days), the severity of the infection has been evaluated visually, and it has been given a rating based on an evaluation scale ranging from 100 (= healthy plant) to 0 (= completely infect plant).

Curative activity.

The leaves of apple-tree, cv. Starking, grown in pot in greenhouse, have been uniformly sprinkled with an aqueous suspension of conidia of *Venturia inaequalis* (200,000 conidia per ccm). After 2 days of permanence in a humidity-saturated environment, said leaves have been treated with the products being tested in a water-acetonic solution at 20% (v/v) of acetone, by sprinkling of both their faces.

At the end of the incubation time (14 days), the severity of the infection has been evaluated visually, and it has been given a rating based on an evaluation scale going from 100 (= healthy plant) to 0 (= completely infect plant).

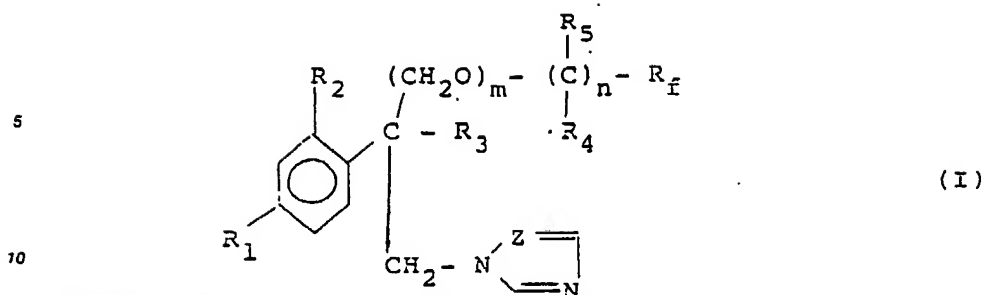
The results are reported in Table 5.

TABLE 5Activity on *Venturia inaequalis* (Cke) Wint.

<u>Compound No.</u>	<u>Dosis, g/l</u>	<u>Preventive Activity</u>	<u>Curative Activity</u>
2	0.05	100	100
penconazole	0.05	88	88
propiconazole	0.05	77	75

Claims

1. Compounds having the general formula:



as well as corresponding salts and metal complexes wherein:

$\underline{m} = 0, 1; \underline{n} = 0, 1;$

$Z = CH, N;$

15 R_1 is selected from chlorine, bromine, fluorine, $-CF_3$, phenyl, C_1 - C_2 -alkoxy, C_1 - C_2 -haloalkoxy, alkylthio, haloalkylthio, wherein the halogen is Cl, Br, F;

R_2 is H, fluorine, chlorine, bromine;

R_3 represents H, CH_3 , CN, or also F when $\underline{m} = 1$ or when $\underline{n} = 1$ and R_4, R_5 are H;

R_4, R_5 are independently H or F;

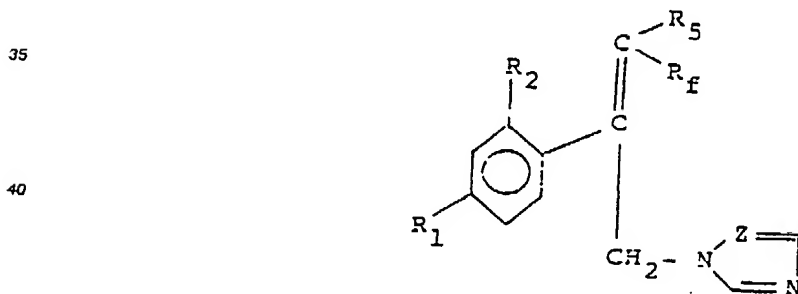
20 R_3 and R_4 , when $\underline{m} = 0$, can furthermore represent, taken together, a second bond between the two carbon atoms to which they are linked in formula (I);

R_1 is selected from the group formed by polyfluoroalkyls, polyfluoroalkenyls and polyfluoroalkynyls containing up to 4 carbon atoms, containing at least 2 F atoms and, optionally, other halogens selected from Cl and Br.

25 2. Compounds according to claim 1, characterized in that \underline{m} is 1, \underline{n} is 0 and R_1 represents an alkyl containing up to 4 carbon atoms, and at least 2 fluorine atoms.

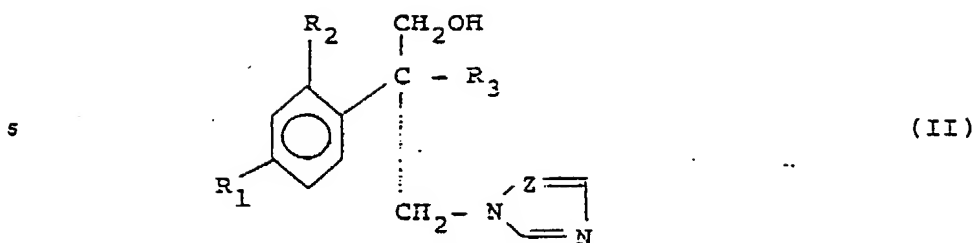
3. Compounds according to claim 1 characterized in that \underline{m} is 0, R_2 is selected from H, CH_3 , CN and R_1 represents an alkyl containing up to 4 carbon atoms and at least 2 fluorine atoms.

30 4. Compounds according to claim 1 characterized in that \underline{m} is 0, \underline{n} is 1, R_3 and R_4 represent, taken together, one bond, R_5 represents H or F, R_1 represents an alkyl containing up to 4 carbon atoms and at least 2 fluorine atoms, having the general formula:



45 5. Compound according to claim 1, which is 1-(1H-1,2,4-triazol-1-yl)-2-(2,4-dichlorophenyl)-3-(1,1,2,2-tetrafluoroethoxy)-propane.

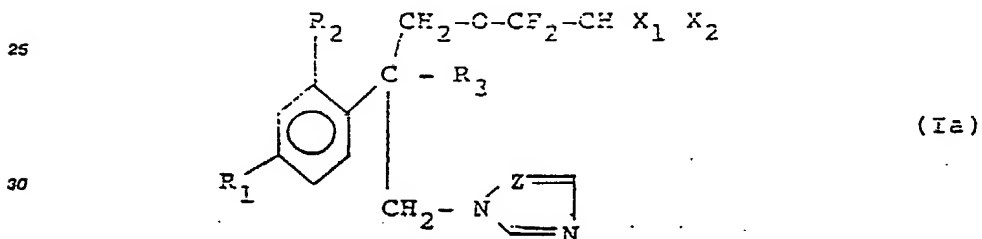
6. Process for the preparation of the compounds defined in claim 2, consisting in reacting an alcohol of formula



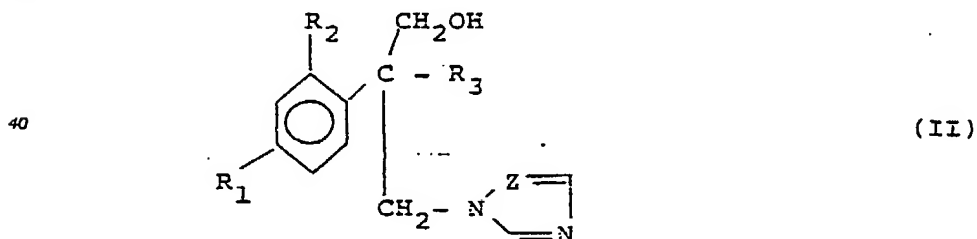
10 wherein R_1 , R_2 , R_3 and Z have the meanings specified in claim 1, with a 1,1-fluoroolefin having the formula



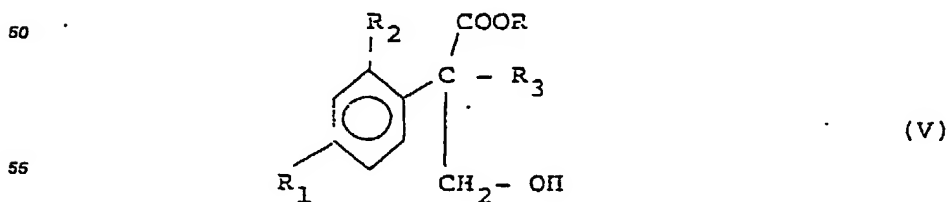
20 wherein X_1 is Cl, F, CF_3 and X_2 is F, CF_3 , in a dipolar aprotic or alcoholic solvent, in the presence of catalytic amounts or of stoichiometric amounts of a strong base, at temperatures comprised within the range of from 20°C to 100°C , to yield the compounds of formula:



35 7. Process for the preparation of the alcohols of formula:

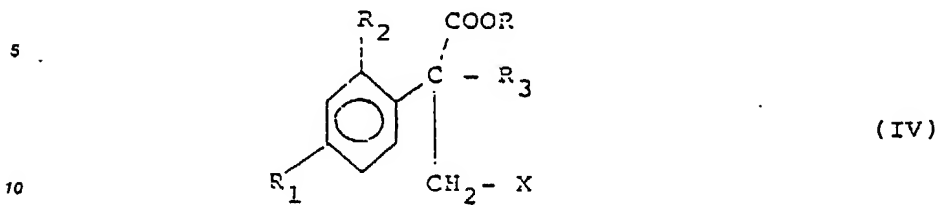


wherein: $R_3 = \text{H, CH}_3, \text{F}$ and R_1, R_2 and Z have the meanings as specified in claim 1, consisting in reacting an ester of formula:



wherein R is CH_3 or C_2H_5 , with a halogenating or mesylating or tosylating agent, according to known

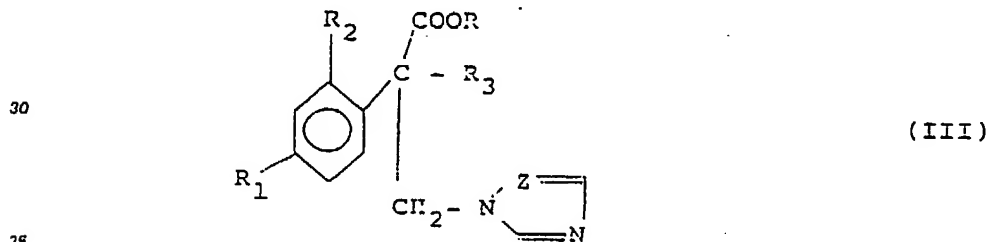
modalities, in subsequently condensing the intermediate obtained, having the formula:



wherein X represents a halogen, a mesyl radical or a tosyl radical, with an alkali-metal salt of an azole having the formula:

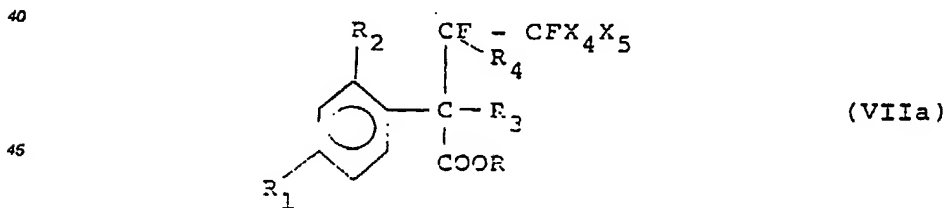


wherein M is an alkali-metal and Z has the previously given meaning, in a dipolar aprotic solvent at temperatures comprised within the range of from 20°C to the reflux temperatures of the reactants, in finally submitting to reduction the intermediate compound so obtained, having the formula:



by using metal hydrides, in ether solvents.

8. Process for the preparation of compounds having the general formula:



wherein R1 and R2 have the meanings indicated in claim 1;

50 R is methyl, ethyl;

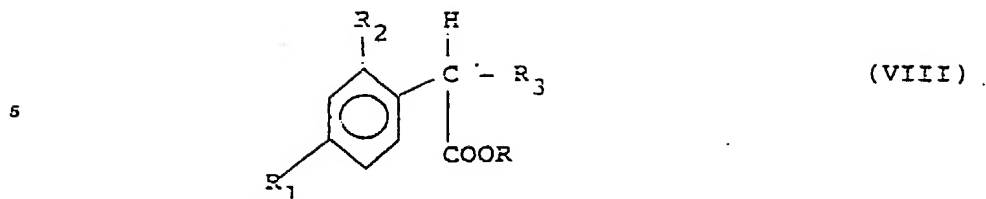
R3 is H, CH3, F

R4 is F;

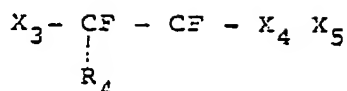
R3 and R4 can furthermore constitute a bond between the carbon atoms they are linked to;

X4 = Br, I;

55 X5 = F, C1-C3 perfluoroalkyl, consisting in reacting the alkali-metal salt, prepared in situ by the action of a strong base on compounds having the general formula:

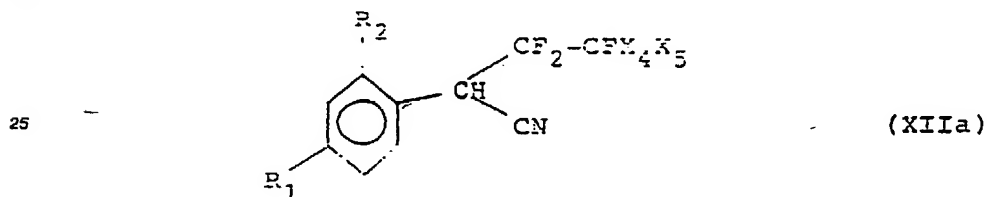


10 with a polyfluoroalkane having the formula:

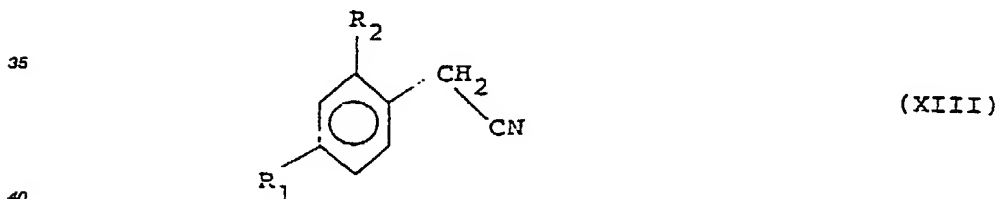


wherein X_3 is Br, I, in a dipolar aprotic or ether solvent, at temperatures comprised within the range of from 20°C to the reflux temperature of the solvent, optionally followed by a dehydrofluorination reaction to yield the unsaturated compounds wherein R_3 and R_4 represent, taken together, a bond.

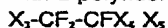
9. Process for the preparation of compounds having the general formula:



25 wherein R_1 , R_2 have the meanings as indicated in claim 1; X_4 is Br, I; X_5 is F, C_1 - C_2 -perfluoroalkyl, consisting in reacting a compound of formula:



with a polyfluoroalkane of formula:



45 wherein X_3 is Br, I, in the presence of a strong base, in a dipolar aprotic solvent, at temperatures comprised within the range of from 20°C to the reflux temperatures of the solvent.

10. Method for combating fungal infestations in useful plants consisting in distributing on the plant, on the seeds or on the surrounding ground, when the fungal infestation is expected or is already in progress, an efficacious amount of a compound according to one or more of the claims 1-5, as such or in the form of a suitable composition.

50 11. Antifungal compositions containing as the active ingredient one or more compounds according to one or more of the claims 1-5 together with a solid or liquid carrier, and possibly other additives.